What is claimed is:

1. A method for the preparation of a peptide-oligonucleotide conjugate (POC), said method comprising the steps of:

a. providing a first N-α-*o*-nitrophenyl sulphenyl (N-α-Nps)-protected amino acid or a first nucleotide;

b. coupling, in any order, at least a second N-α-Nps-protected amino acid and/or at least a second nucleotide to said first N-α-Nps-protected amino acid or said first nucleotide; and

c. repeating step (b) as necessary, so as to form a peptide-oligonucleotide conjugate having at least one amino acid-nucleotide bond;

wherein each coupling step is conducted in the presence of a coupling reagent compatible with peptide synthesis; and

wherein said N-α-Nps protecting group is removed prior to each amino acid-amino acid coupling step using thioacetamide in the presence of dichloroacetic acid.

2. The method according to claim 1, wherein said coupling reagent is selected from the group consisting of 1-hydroxybenzotriazole (HOBt), 3-hydroxy-3,4-dihydro-1,2,3-benzotriazine-4-one (HOOBt), N-hydroxysuccinimide (NHS), dicyclohexylcarbodiimide (DCC), diisopropylcarbodiimide (DIC), 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDAC), 2-(1*H*-7-azabenztriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluoro phosphate (HATU), 2-(1*H*-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), 3,4-dihydro-1,2,3-benzotriazin-4-one-3-oxy-tetramethyluronium hexafluorophosphate (HDTU), benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluoro phosphate (BOP), benzotriazol-1-yloxytris-(pyrrolidino)-pjosphonium hexafluoro phosphate (PyBop), (3,4-dihydro-1,2,3-benzotriazin-4-one-3-oxy) diethyl phosphate (DEPBt), 3,4-dihydro-1,2,3-benzotriazin-4-one-3-oxy- yloxytris-(pyrrolidino)-pjosphonium hexafluoro phosphate (PDOP), 2-(benzotriazol-1-yloxy)-1,3-dimethyl-2-pyrrolidin-1-yl-

1,3,2-diazaphospholidinium hexafluorophosphonate (BOMP), 5-(1H-7-azabenzotriazol-l-yloxy)-3,4-dihydro-l-methyl 2H-pyrrolium hexachloroantimonate (AOMP), (1H-7-azabenzotriazol-1-yloxy)tris(dimethylamino) phosphonium hexafluoroposphate (AOP), 5-(1H-Benzotriazol-1-yl)-3,4-dihydro-1-methyl 2H-pyrrolium hexachloroantimonate: N-oxide (BDMP), 2-bromo-3-ethyl-4-methyl thiazolium tetrafluoroborate (BEMT), 2-bromo-1-ethyl pyridinium tetrafluoroborate (BEP), 2-bromo-1-ethyl pyridinium hexachloroantimonate (BEPH), N-(1H-benzotriazol-1-ylmethylene)-N-methylmethanaminium hexachloroantimonate N-oxide (BOMI), N,N'-bis(2-oxo-3-oxazolidinyl) phosphinic chloride (BOP-Cl), 1-(1H-benzotriazol-1-yloxy)phenylmethylene pyrrolidinium hexachloroantimonate (BPMP), 1,1,3,3-bis(tetramethylene) fluorouronium hexafluorophosphate (BTFFH), chloro(4-morphoino)methylene morpholinium hexafluorophosphate (CMMM), 2-chloro-1,3-dimethyl-1H-benzimidazolium hexafluorophosphate (CMBI), 2-fluoro-1-ethyl pyridinium tetrafluoroborate (FEP), 2-fluoro-1-ethyl pyridinium hexachloroantimonate (FEPH), 1-(1-pyrrolidinyl-1H-1,2,3-triazolo[4,5-b]pyridin-1-ylmethylene)pyrrolidinium hexafluorophosphate N-oxide (HAPyU), O-(1H-benzotriazol-l-yl)-N,N,N',N;-bis(pentamethylene)uronium hexafluorophosphate (HBPipU), O-(1H-benzotriazol-1-yl)-N,N,N0,N0-bis(tetramethylene)urinium hexafluorophosphate (HBPyU), (1H-7-azabenzotriazol-1-yloxy)tris(pyrrolidino)phosphonium hexafluorophosphate (PyAOP), bromotripyrrolidinophosphonium hexafluorophosphate (PyBrop), chlorotripyrrolidinophosphonium hexafluorophosphate (PyCloP), 1,1,3,3-bis(tetramethylene) chlorouronium hexafluorophosphate (PyClU), tetramethylfluoromamidinium hexafluorophosphate (TFFH), triphosgene, triazine-based reagents [cyanuric chloride, cyanuric fluoride, 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMT-MM), 2-chloro-4,6-dimethoxy-

1,3,5-triazine (CDMT)], bis(2-chlorophenyl) phosphorochloridate, diphenyl phosphorochloridate, diphenyl phosphoroazide (DPPA), and any combination thereof

3. The method according to claim 1, wherein said coupling reagent is 2-(1*H*-7-azabenztriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluoro phosphate (HATU).

4. The method according to claim 1, wherein said coupling reagent is 3,4-dihydro-1,2,3-benzotriazin-4-one-3-oxy-tetramethyluronium hexafluorophosphate (HDTU).

5. The method according to claim 1, wherein said coupling reagent is N,N'-bis(2-oxo-3-oxazolidinyl) phosphinic chloride (BOP-Cl).

6. The method according to claim 1, wherein said coupling reagent is an organophosphoro halogenate or a pseudohalogenate.

7. The method according to claim 6, wherein said coupling reagent is diphenyl phosphorochloridate.

8. The method according to claim 6, wherein said coupling reagent is diphenylphosphoroazide (DPPA).

9. The method according to claim 1, wherein said coupling reagent is a halogeno tris(organo)phosphonium hexafluoro phosphate.

10. The method according to claim 9, wherein said coupling reagent is bromo tris(dimethylamino)phosphonium hexafluoro phosphate (BrOP).

11. The method according to claim 9, wherein said coupling reagent is chlorotris(dimethylamino)phosphonium hexafluoro phosphate (ClOP).

12. The method according to claim 9, wherein said coupling reagent is bromotripyrrolidinophosphonium hexafluorophosphate (PyBrop).

13. The method according to claim 9, wherein said coupling reagent is chlorotripyrrolidinophosphonium hexafluorophosphate (PyClop).

14. The method according to claim 1, wherein said N-α-Nps-protected amino acid is selected from the group consisting of an N-α-Nps-protected glycine, alanine, valine, leucine, isoleucine, proline, arginine, lysine, histidine, serine, threonine, aspartic acid, glutamic

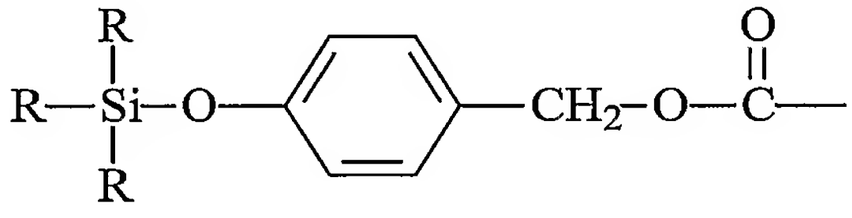
acid, asparagine, glutamine, cysteine, homocysteine, cystine, methionine, ornithine, norleucine, phenylalanine, tyrosine, tryptophan, beta-alanine, homoserine, homoarginine, isoglutamine, pyroglutamic acid, gamma-aminobutryic acid, citrulline, sarcosine, and statine.

15. The method according to claim 1, wherein said N-α-Nps-protected amino acid is a side-chain protected amino acid.

16. The method according to claim 15, wherein said side-chain protected amino acid is selected from the group consisting of arginine, lysine, aspartic acid, asparagine, glutamic acid, glutamine, histidine, cysteine, homocysteine, ornithine, serine, homoserine, threonine, homoarginine, citrulline and tyrosine.

17. The method according to claim 15, wherein said side chain protecting group is a silyl protecting group of the formula $(R)_4Si$ wherein each R is independently of the other an unsubstituted or substituted alkyl, alkylaryl, aryl, oxyalkyl, oxyalkylaryl, or oxyaryl.

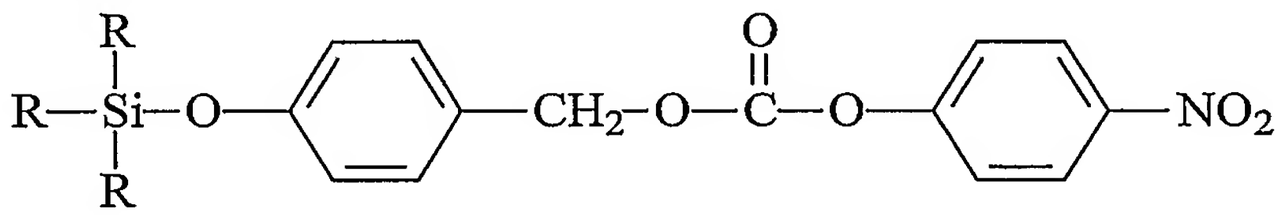
18. The method according to claim 15, wherein said side chain protecting group is represented by the structure:



wherein each R is independently of the other selected from the group consisting of an unsubstituted or substituted alkyl, alkylaryl, aryl, oxyalkyl, oxyalkylaryl and oxyaryl.

19. The method according to claim 18, wherein R is isopropyl.

20. The method according to claim 18, wherein said side-chain protected amino acid is prepared by coupling said side chain with a compound of the formula:



(III)

21. The method according to claim 15, wherein said side-chain protecting group is Fmoc.

22. The method according to claim 15, wherein said side-chain protecting group is an Fm ester.

23. The method according to claim 1, wherein each nucleotide-nucleotide coupling step is conducted by phosphate coupling, H-phosphonate coupling or phosphate coupling, or any combination thereof.

24. The method according to claim 1, wherein each nucleotide-nucleotide coupling step is conducted by H-phosphonate coupling.

25. The method according to claim 1, wherein said POC is prepared on a solid support.

26. The method according to claim 1, wherein said oligonucleotide is synthesized first.

27. The method according to claim 1, wherein said peptide is synthesized first.

28. The method according to claim 1, wherein said peptide and said oligonucleotide are synthesized in alternating sequences.

29. A method for the preparation of a peptide-oligonucleotide conjugate (POC), said method comprising the steps of:

a. providing a first N-α-o-nitrophenyl sulphenyl (N-α-Nps)-protected amino acid or a first nucleotide;

b. coupling, in any order, at least a second N-α-Nps-protected amino acid and/or at least a second nucleotide to said first N-α-Nps-protected amino acid or said first nucleotide; and

c. repeating step (b) as necessary, so as to form a peptide-oligonucleotide conjugate having at least one amino acid-nucleotide bond;

wherein each coupling step is conducted in the presence of a coupling reagent compatible with peptide synthesis;

wherein said N-α-Nps protecting group is removed prior to each amino acid-amino acid coupling step using thioacetamide in the presence of dichloroacetic acid; and

wherein each nucleotide-nucleotide coupling step is conducted by H-phosphonate coupling.

30. The method according to claim 29, wherein said coupling reagent is selected from the group consisting of 1-hydroxybenzotriazole (HOBt), 3-hydroxy-3,4-dihydro-1,2,3-benzotriazine-4-one (HOOBt), N-hydroxysuccinimide (NHS), dicyclohexylcarbodiimide (DCC), diisopropylcarbodiimide (DIC), 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDAC), 2-(1*H*-7-azabenztriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluoro phosphate (HATU), 2-(1*H*-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), 3,4-dihydro-1,2,3-benzotriazin-4-one-3-oxy-tetramethyluronium hexafluorophosphate (HDTU), benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluoro phosphate (BOP), benzotriazol-1-yloxytris-(pyrrolidino)-pjosphonium hexafluoro phosphate (PyBop), (3,4-dihydro-1,2,3-benzotriazin-4-one-3-oxy) diethyl phosphate (DEPBt), 3,4-dihydro-1,2,3-benzotriazin-4-one-3-oxy- yloxytris-(pyrrolidino)-pjosphonium hexafluoro phosphate (PDOP), 2-(benzotriazol-1-yloxy)-1,3-dimethyl-2-pyrrolidin-1-yl-1,3,2-diazaphospholidinium hexafluorophosphonate (BOMP), 5-(1H-7-azabenzotriazol-l-yloxy)-3,4-dihydro-l-methyl 2H-pyrrolium hexachloroantimonate (AOMP), (1H-7-azabenzotriazol-1-yloxy)tris(dimethylamino) phosphonium hexafluoroposphate (AOP), 5-(1H-Benzotriazol-1-yl)-3,4-dihydro-1-methyl 2H-pyrrolium hexachloroantimonate: N-oxide (BDMP), 2-bromo-3-ethyl-4-methyl thiazolium tetrafluoroborate (BEMT), 2-bromo-1-ethyl pyridinium tetrafluoroborate (BEP), 2-bromo-1-ethyl pyridinium hexachloroantimonate (BEPH), N-(1H-benzotriazol-1-ylmethylene)-N-methylmethanaminium hexachloroantimonate N-oxide (BOMI), N,N'-bis(2-oxo-3-oxazolidinyl) phosphinic chloride (BOP-Cl), 1-(1H-benzotriazol-1-yloxy)phenylmethylene pyrrolidinium

hexachloroantimonate (BPMP), 1,1,3,3-bis(tetramethylene) fluorouronium hexafluorophosphate (BTFFH), chloro(4-morphoino)methylene morpholinium hexafluorophosphate (CMMM), 2-chloro-1,3-dimethyl-1H-benzimidazolium hexafluorophosphate (CMBI), 2-fluoro-1-ethyl pyridinium tetrafluoroborate (FEP), 2-fluoro-1-ethyl pyridinium hexachloroantimonate (FEPH), 1-(1-pyrrolidinyl-1H-1,2,3-triazolo[4,5-b]pyridin-1-ylmethylene)pyrrolidinium hexafluorophosphate N-oxide (HAPyU), O-(1H-benzotriazol-l-yl)-N,N,N',N;-bis(pentamethylene)uronium hexafluorophosphate (HBPipU), O-(1H-benzotriazol-1-yl)-N,N,N0,N0-bis(tetramethylene)urinium hexafluorophosphate (HBPyU), (1H-7-azabenzotriazol-1-yloxy)tris(pyrrolidino)phosphonium hexafluorophosphate (PyAOP), bromotripyrrolidinophosphonium hexafluorophosphate (PyBrop), chlorotripyrrolidinophosphonium hexafluorophosphate (PyCloP), 1,1,3,3-bis(tetramethylene) chlorouronium hexafluorophosphate (PyClU), tetramethylfluoromamidinium hexafluorophosphate (TFFH), triphosgene, triazine-based reagents [cyanuric chloride, cyanuric fluoride, 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMT-MM), 2-chloro-4,6-dimethoxy-1,3,5-triazine (CDMT)], bis(2-chlorophenyl) phosphorochloridate, diphenyl phosphorochloridate, diphenyl phosphoroazide (DPPA), and any combination thereof

31. The method according to claim 29, wherein said coupling reagent is 2-(1*H*-7-azabenztriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluoro phosphate (HATU).

32. The method according to claim 29, wherein said coupling reagent is 3,4-dihydro-1,2,3-benzotriazin-4-one-3-oxy-tetramethyluronium hexafluorophosphate (HDTU).

33. The method according to claim 29, wherein said coupling reagent is N,N'-bis(2-oxo-3-oxazolidinyl) phosphinic chloride (BOP-Cl).

34. The method according to claim 29, wherein said coupling reagent is an organophosphoro halogenate or a pseudohalogenate.

35. The method according to claim 34, wherein said coupling reagent is diphenyl phosphorochloridate.

36. The method according to claim 34, wherein said coupling reagent is diphenylphosphoroazide (DPPA).

37. The method according to claim 29, wherein said coupling reagent is a halogeno tris(organo)phosphonium hexafluoro phosphate.

38. The method according to claim 37, wherein said coupling reagent is bromo tris(dimethylamino)phosphonium hexafluoro phosphate (BrOP).

39. The method according to claim 37, wherein said coupling reagent is chlorotris(dimethylamino)phosphonium hexafluoro phosphate (ClOP).

40. The method according to claim 37, wherein said coupling reagent is bromotripyrrolidinophosphonium hexafluorophosphate (PyBrop).

41. The method according to claim 37, wherein said coupling reagent is chlorotripyrrolidinophosphonium hexafluorophosphate (PyClop).

42. The method according to claim 29, wherein said N-α-Nps-protected amino acid is selected from the group consisting of an N-α-Nps-protected glycine, alanine, valine, leucine, isoleucine, proline, arginine, lysine, histidine, serine, threonine, aspartic acid, glutamic acid, asparagine, glutamine, cysteine, homocysteine, cystine, methionine, ornithine, norleucine, phenylalanine, tyrosine, tryptophan, beta-alanine, homoserine, homoarginine, isoglutamine, pyroglutamic acid, gamma-aminobutryic acid, citrulline, sarcosine, and statine.

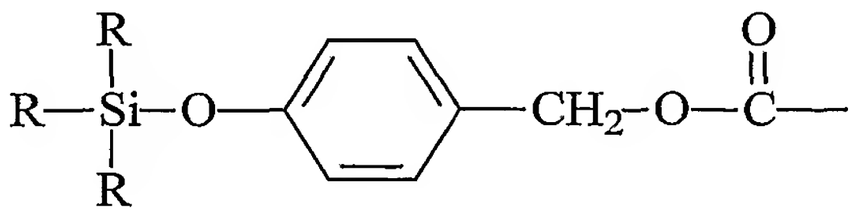
43. The method according to claim 29, wherein said N-α-Nps-protected amino acid is a side-chain protected amino acid.

44. The method according to claim 43, wherein said side-chain protected amino acid is selected from the group consisting of arginine, lysine, aspartic acid, asparagine, glutamic acid, glutamine, histidine,

cysteine, homocysteine, ornithine, serine, homoserine, threonine, homoarginine, citrulline and tyrosine.

45. The method according to claim 43, wherein said side chain protecting group is a silyl protecting group of the formula $(R)_4Si$ wherein each R is independently of the other an unsubstituted or substituted alkyl, alkylaryl, aryl, oxyalkyl, oxyalkylaryl, or oxyaryl.

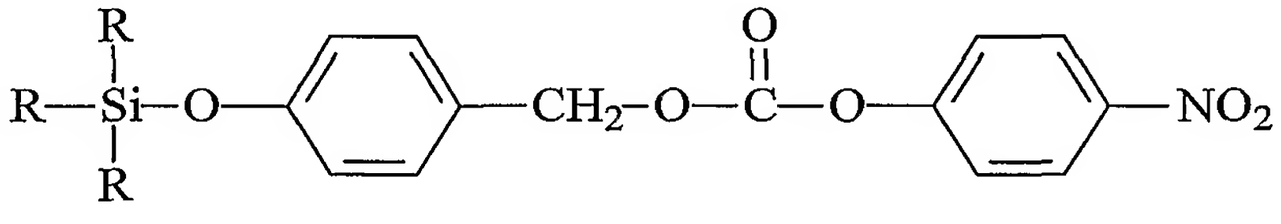
46. The method according to claim 43, wherein said side chain protecting group is represented by the structure:



wherein each R is independently of the other selected from the group consisting of an unsubstituted or substituted alkyl, alkylaryl, aryl, oxyalkyl, oxyalkylaryl and oxyaryl.

47. The method according to claim 46, wherein R is isopropyl.

48. The method according to claim 46, wherein said side-chain protected amino acid is prepared by coupling said side chain with a compound of the formula:



(III)

49. The method according to claim 43, wherein said side-chain protecting group is Fmoc.

50. The method according to claim 43, wherein said side-chain protecting group is an Fm ester.

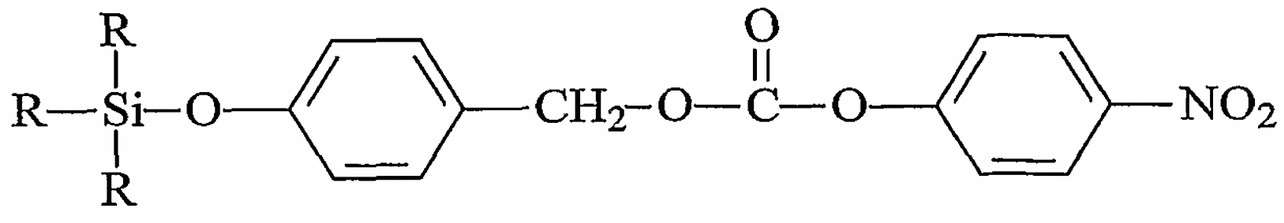
51. The method according to claim 29, wherein said POC is prepared on a solid support.

52. The method according to claim 29, wherein said oligonucleotide is synthesized first.

53. The method according to claim 29, wherein said peptide is synthesized first.

54. The method according to claim 29, wherein said peptide and said oligonucleotide are synthesized in alternating sequences.

55. A compound represented by the structure:



(III)

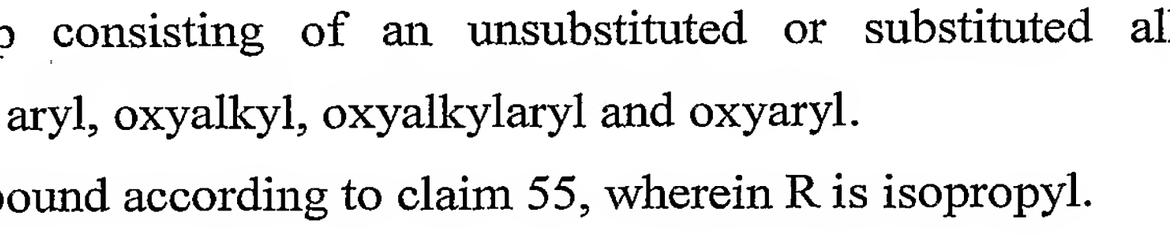
wherein each R is independently of the other selected from the group consisting of an unsubstituted or substituted alkyl, alkylaryl, aryl, oxyalkyl, oxyalkylaryl and oxyaryl.

56. The compound according to claim 55, wherein R is isopropyl.

57. Use of a compound according to claim 55 for the protection of the side chain of an amino acid.

58. Use according to claim 57, wherein the amino acid is selected from the group consisting of arginine, lysine, aspartic acid, asparagine, glutamic acid, glutamine, histidine, cysteine, homocysteine, ornithine, serine, homoserine, threonine, homoarginine, citrulline and tyrosine.

59. A side-chain protected amino acid represented by the structure:



(I)

wherein

A represents a side chain residue of said amino acid;

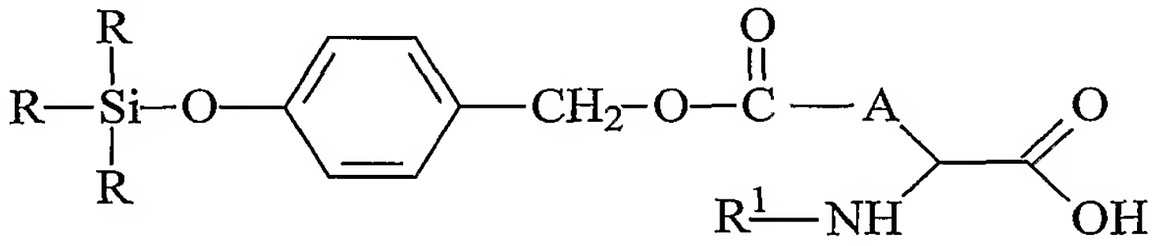
R is independently selected from the group consisting of an unsubstituted or substituted alkyl, alkylaryl, aryl, oxyalkyl, oxyalkylaryl and oxyaryl; and

R^1 represents hydrogen or an amino protecting group.

60. The side-chain protected amino acid according to claim 59, wherein said amino acid is selected from the group consisting of arginine, lysine, aspartic acid, asparagine, glutamic acid, glutamine, histidine, cysteine, homocysteine, ornithine, serine, homoserine, threonine, homoarginine, citrulline and tyrosine.

61. The side-chain protected amino acid according to claim 59, wherein R^1 is o-nitrophenyl sulphenyl (Nps).

62. A method for preparing a side-chain protected amino acid of the formula:



(I)

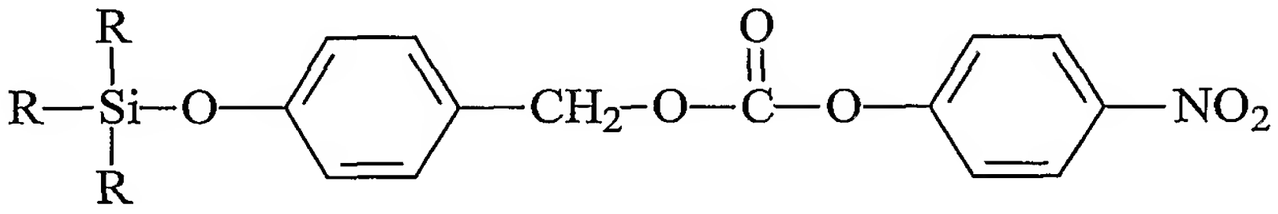
wherein

A represents a side chain residue of said amino acid;

R is independently selected from the group consisting of an unsubstituted or substituted alkyl, alkylaryl, aryl, oxyalkyl, oxyalkylaryl and oxyaryl; and

R^1 represents hydrogen or an amino protecting group;

said method comprising the step of reacting said amino acid with a compound of the formula:



(III)

thereby forming said side-chain protected amino acid.

63. The method according to claim 62, wherein said amino acid is selected from the group consisting of arginine, lysine, aspartic acid, asparagine, glutamic acid, glutamine, histidine, cysteine,

homocysteine, ornithine, serine, homoserine, threonine, homoarginine, citrulline and tyrosine.

64. The method according to claim 62, wherein R^1 is o-nitrophenyl sulphenyl (Nps).

65. A method for the preparation of a peptide-oligonucleotide conjugate (POC), said method comprising the step of:

performing at least one coupling between an α-amino protected amino acid and a nucleotide so as to form a peptide-oligonucleotide conjugate having at least one amino acid-nucleotide bond;

wherein said amino acid or nucleotide further comprise one or more orthogonal protecting groups where required;

wherein each coupling step is conducted in the presence of a coupling reagent compatible with peptide synthesis; and

wherein said α-amino protecting group is removed prior to each amino acid-amino acid coupling step using a deprotecing agent compatible with any one or more protecting groups present in the oligonucleotide-peptide conjugate.

66. The method according to claim 65, wherein said α-amino protecting group is N-α-*o*-nitrophenyl sulphenyl (N-α-Nps).

67. The method according to claim 65, wherein said α-amino protecting group is *p*-azidobenzyloxycarbonyl (ACBZ).

68. A method for the preparation of a peptide-oligonucleotide conjugate (POC), said method comprising the step of performing at least one coupling between an N-α-*o*-nitrophenyl sulphenyl (N-α-Nps) amino acid and a nucleotide so as to form a peptide-oligonucleotide conjugate having at least one amino acid-nucleotide bond;

wherein said N-α-Nps protected amino acid or nucleotide further comprise one or more orthogonal protecting groups where required;

wherein each coupling step is conducted in the presence of a coupling reagent compatible with peptide synthesis; and

wherein said N-α-Nps protected amino protecting group is removed prior to each amino acid-amino acid coupling step using a deprotecing agent compatible with any one or more protecting groups present in the oligonucleotide-peptide conjugate.

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